

Possibilities for flexible manufacturing capabilities for multi-product use

Kim L. Nelson, Ph.D.
CRB Consulting Engineers

International Vaccine Technology Workshop

17–18 September 2010

Hyderabad, India

Topics

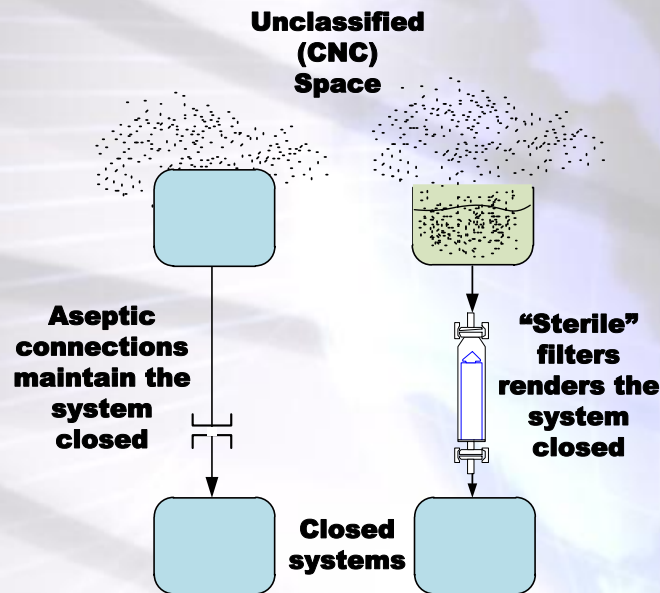
- Current gaps in vaccine manufacturing capacity
- Enabling Technologies
- FutureFacility
 - Responsive facilities providing increased flexibility / adaptability, providing a fast response to changing needs such as number of doses, titer, strain or process
 - Reduced capital cost
 - Reduced time to market
- Sustainable vaccine production capacity.

current gaps in developing countries' vaccine capacity

- Fundable initial capital investment costs
- GMP compliance
- Acceptable cost of goods
- Flexibility
 - Adaptability for deploying of new processes
 - Expandability for surge demands
- Experience with available enabling technologies

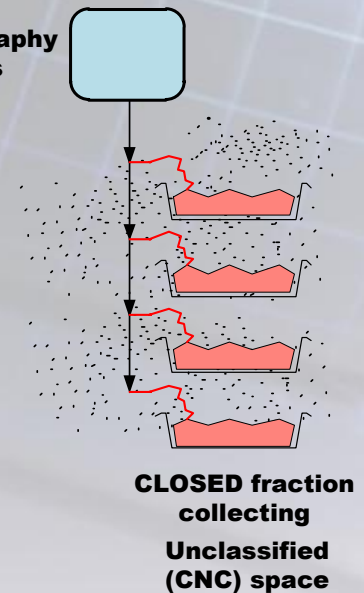
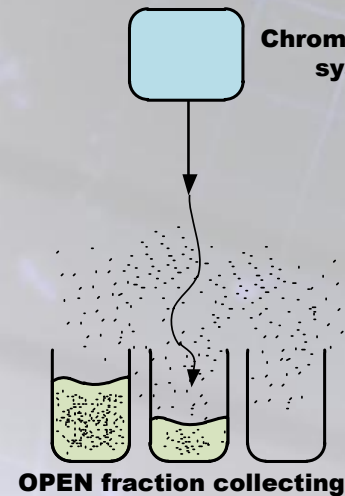
System Closure an Enabling Technology

- Very important principle
- Adopted in ISPE Baseline Guide for Biopharmaceutical Facilities
- With a closed process, you can lower the room classification

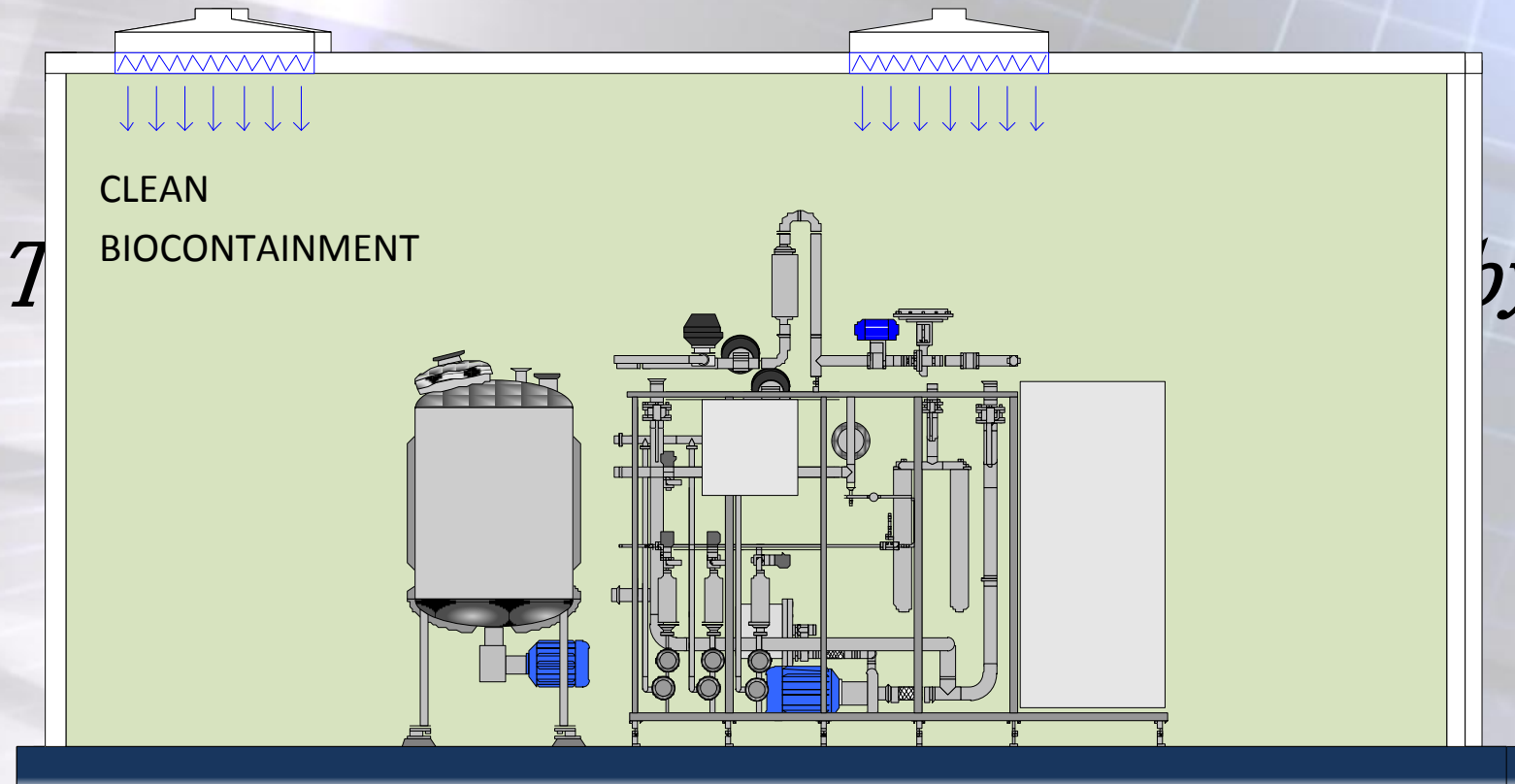


**Typical of
cell culture
or fermentation**

**Typical of
buffer or
media prep**

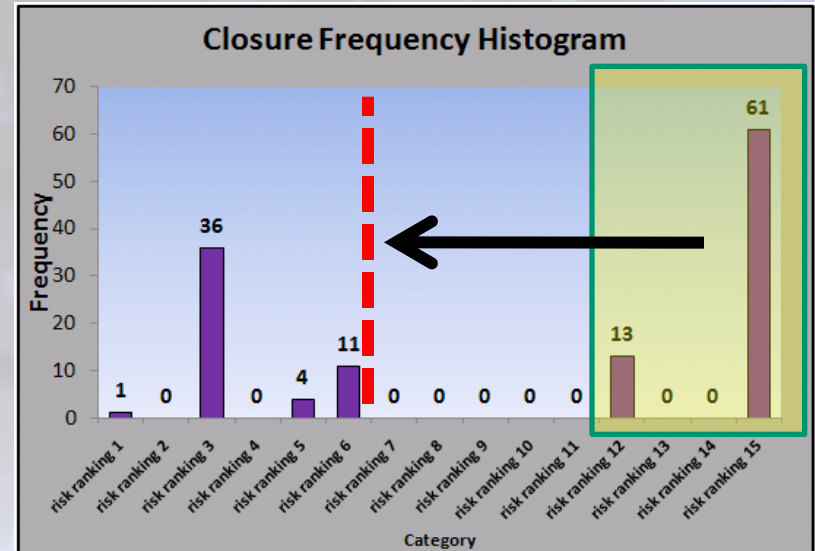
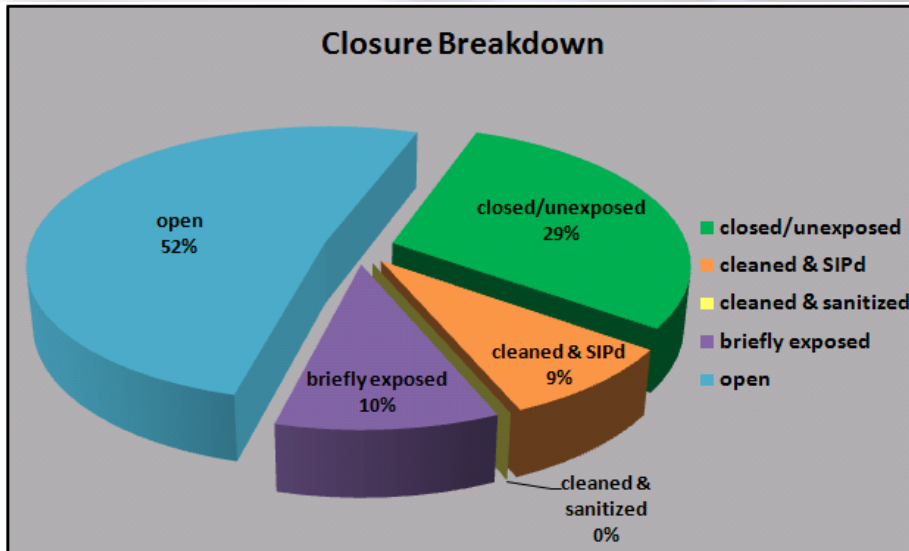


Bioreactors in cleanroom areas what do you gain?



Closure Analysis identifies risks

- **Method:** Excel-based tool for the systematic evaluation of process closure and required level of bioburden control
- **Output:** Risk ranking for each process step based on environmental risk
- **Impact:** Develop conceptual design that is consensus-based & mitigates potential product and intermediate quality risks

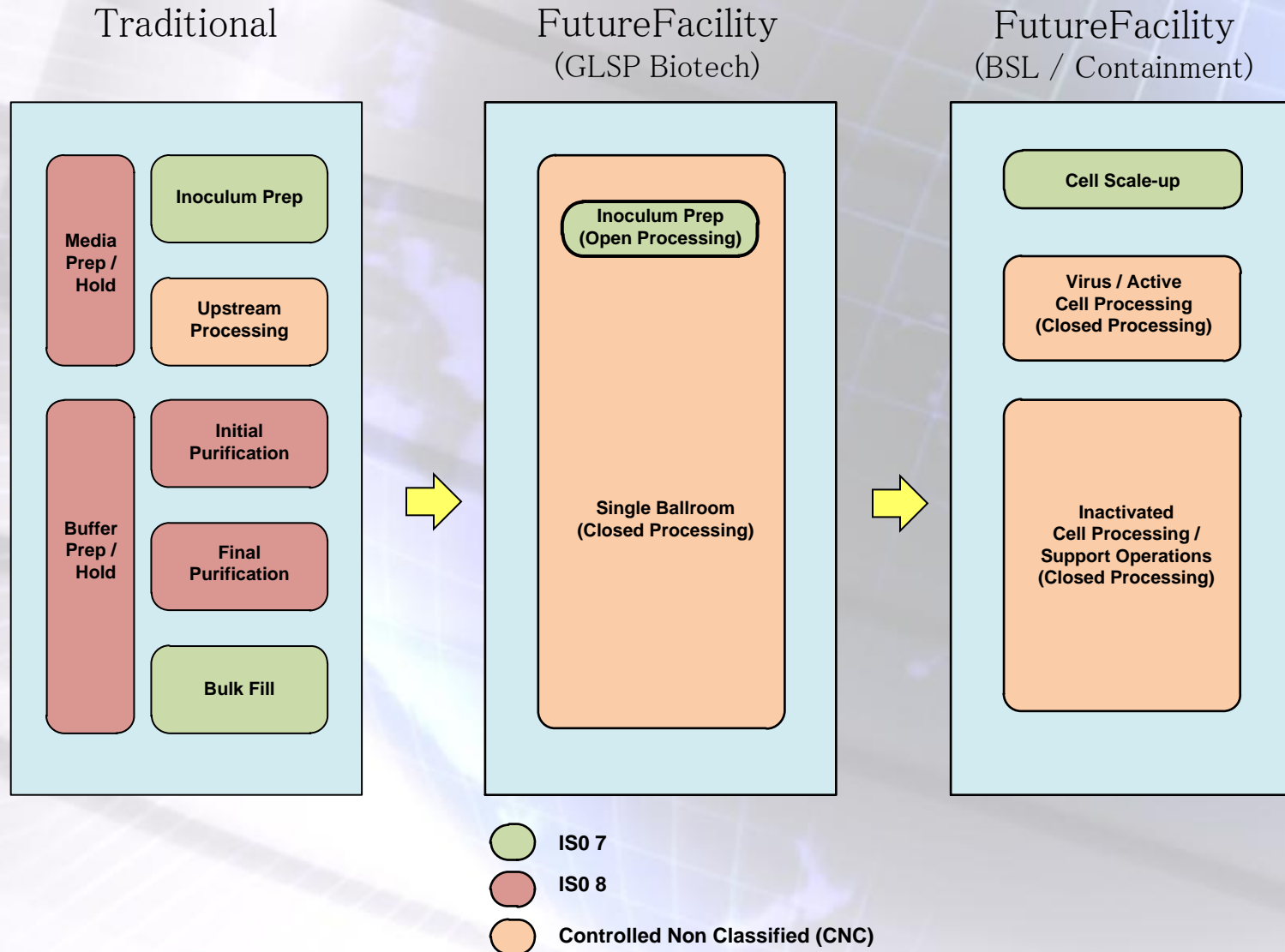


Low Risk

High Risk



Impact of Closed Processing



Single use systems an Enabling Technology



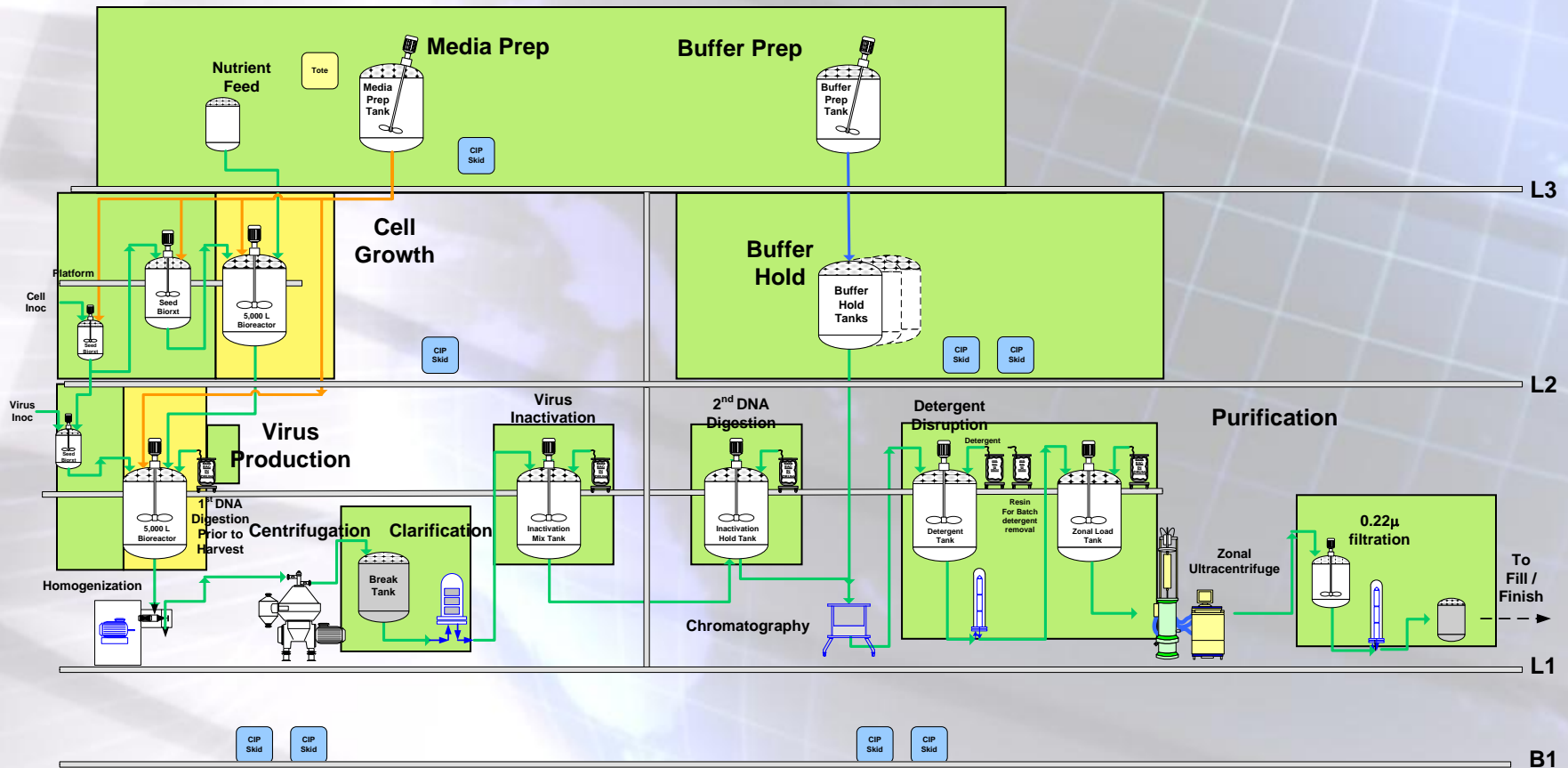
Single-Use Systems Advantages

- Process flexibility
- Lower initial capital cost
- Faster time to market
- Decreased water demand
- Faster product changeovers
- Labor savings potential
- Decreased wastewater discharge
- Decreased cleaning & sterilization validation

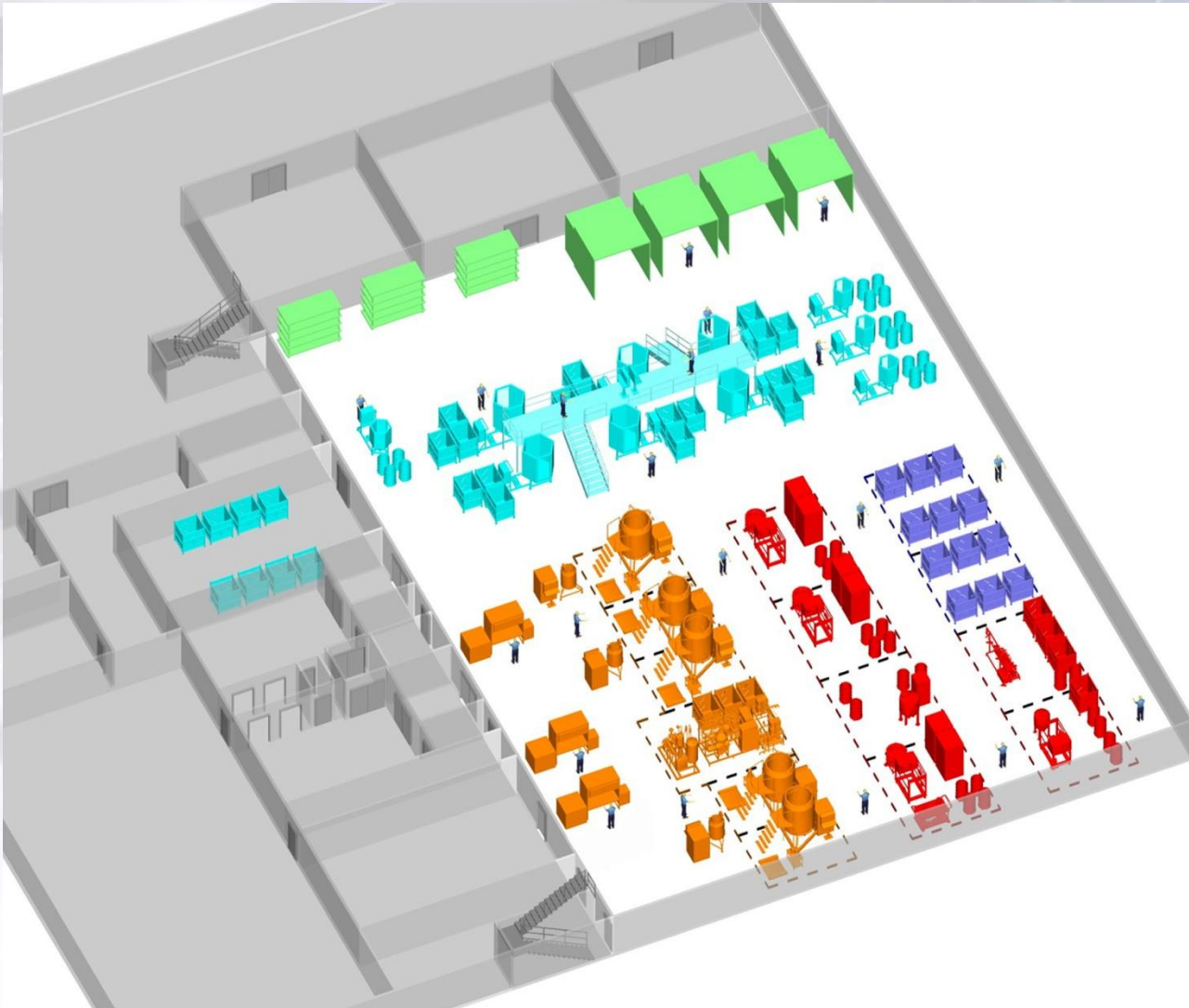
Single-Use Systems Issues

- Possible process scale limitations
- Ongoing operating expenses for disposables
- Extractable , Leachable & Product contact validation
- More corridor & airlock space required
- More staging & storage spaces required
- Solid waste disposal
- Supply Chain management
 - Importation
 - Multiple suppliers
 - Inventory levels
 - Custom Options in bags
- Larger Warehouse inventories for disposable supplies
- Bag-tubing manifolds must all be configured & go thru procurement process prior to start-up

Opportunities for single-use systems in Influenza vaccine mfg

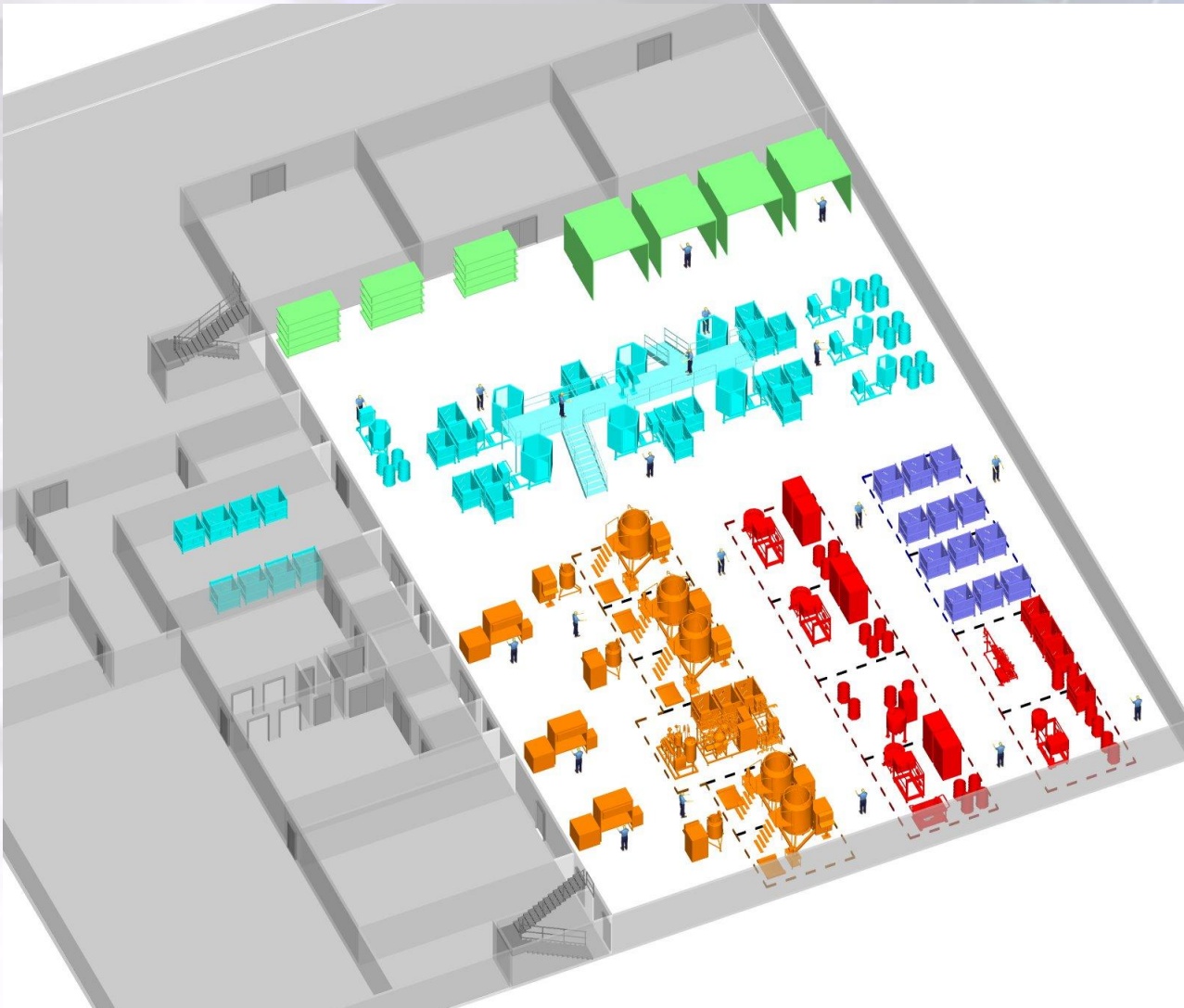


Handling biocontainment



Responsive facilities

Modularity of Plug-and-Play Operation
provides great manufacturing flexibility



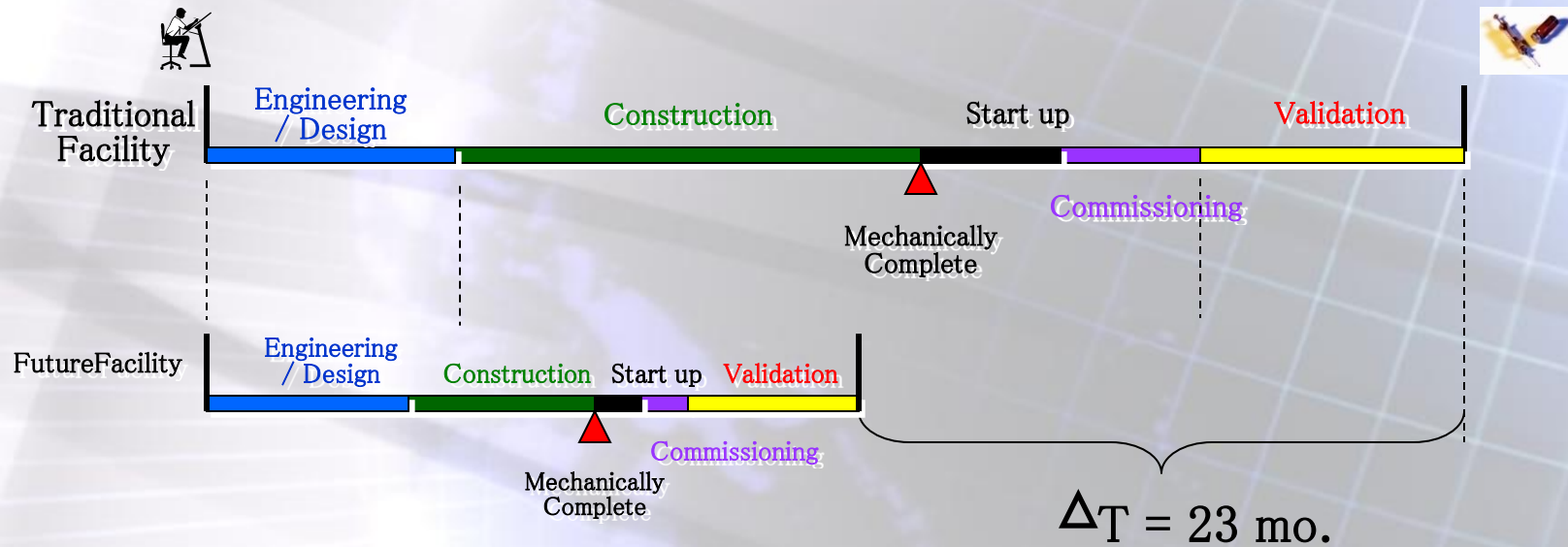
Benefits of closed processing & Future Facility Concepts

- Reduced manufacturing area (15–30%)
- Reduced HVAC
 - Reduced room classifications
 - Reduced cleanroom areas
 - Reduced air changes per hours
 - Reduced fan power demand
 - Reduced number of air handling units
 - Reduced maintenance

Benefits of closed processing & Future Facility Concepts

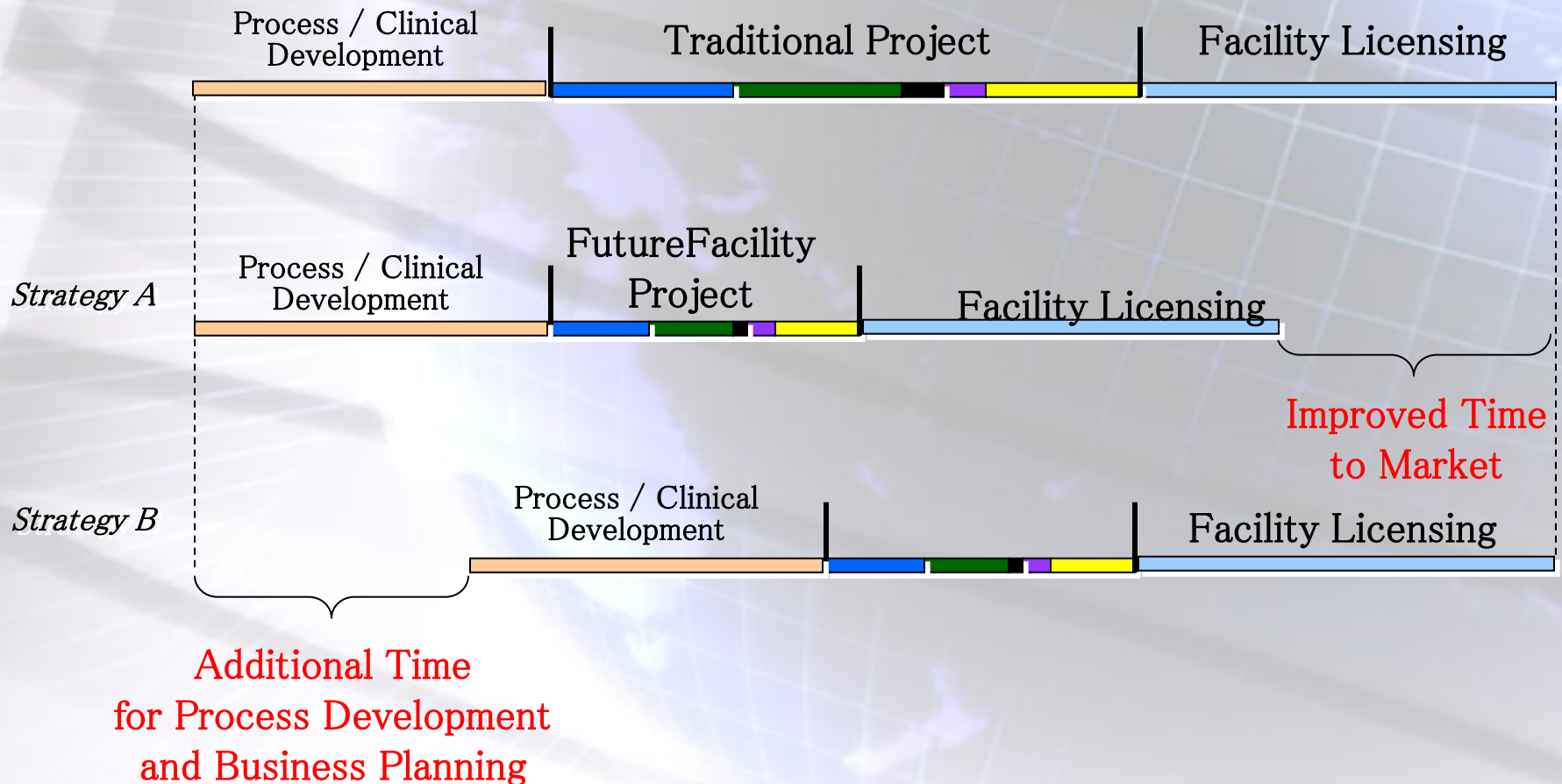
- Reduced Utilities
 - Using single use systems can reduce clean steam and WFI requirements (up to 80–90% reductions)
 - Reduced chilled water and steam demands (up to 60% savings)
 - Reduced wastewater
- Reduced Construction & Start-up Schedule
 - Up to 50% schedule savings
- Reduced COGs (situation dependent)

Reduced time to market



	Traditional	FutureFacility	% Change
SCHEDULE	Months	Months	
Engineering / Design	9	6	-33%
Construction / Mech Completion	18	6	-67%
Start-up	3	2	-33%
Commissioning	6	2	-67%
Validation	12	9	-25%
Totals	48	25	-48%

Quicker Project Timeline Allows Options



Summary

- **Flexible, Adaptable & Expandable** facilities are possible and cost effective
- **Process Closure** provides superior product protection AND allows lower room classifications
- **Single-Use systems** offer process flexibility, shortened construction schedule and start-up/validation schedule, and decreased utilities



Thank you for your attention !

Kim L. Nelson, Ph.D.
Director
CRB Consulting Engineers
220 W. Germantown Pike, Suite 170
Plymouth Meeting, PA 19462
USA

(610)-278-7644 office
(215)-435-0390 cell
kim.nelson@crbusa.com